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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/931,112	08/17/2001	Marshall Z. Schwartz	06510003PB	3767

7590 07/29/2005
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EXAMINER

BORIN, MICHAEL L

ART UNIT PAPER NUMBER

1631

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/931,112

Applicant(s)

SCHWARTZ, MARSHALL Z.

Examiner

Michael Borin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 May 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7,9-12 and 21-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7,9-12, 21-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

8.00

DETAILED ACTION

Status of the application

Appeal Brief filed 05/18/2005 is acknowledged. Upon further consideration, it was deemed that the Declaration under 37 CFR 1.131 filed after final, on 01/25/2005, is sufficient to overcome art rejection of record. Consequently, the rejection of record is vacated and a new ground of rejections is deemed necessary. The finality of the Office action mailed 07/26/2004 is hereby withdrawn.

Claims 7,9-12, 21-33 are pending.

Claim Rejections - 35 U.S.C. 103

Claims 7,9-12, 21-33 are rejected under 35 U.S.C. 103(a) as being obvious over Bozkurt et al (J Clin Ultrasound. 1994 Feb;22(2):85-91) in view of Dignass et al (and Nasrat et al (Journal of Clinical Investigation, 93(5), 2056-2065, 1994).

The instant invention is drawn to method of treating intestinal mucosal damage in a patient suffering from inflammatory bowel disease comprising decreasing mucosal damage in a small intestine by administering an effective dose of hepatocyte growth factor (HGF).

Bozkurt et al teach that patients having inflammatory bowel disease suffer from pathological lesions of intestine. See abstract.

Dignass et al teach that it is known that growth factors have been demonstrated to play important role in modulation of intestinal epithelial restitution, both *in vitro* and *in vivo*. Dignass et al demonstrate that HGF stimulates two intestinal epithelial cell

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functions: proliferation and restitution, the latter is a process that rapidly re-establishes mucosal integrity after an injury by rapid migration of epithelial cells across the wound margin. See abstract, p. 702, second paragraph, pages 703-705. Stimulation of cell proliferation is demonstrated on p. 703 and Fig. 1. p. 704 and fig 2 demonstrate effect of HGF on cell restitution in an *in vitro* model. Both effects are dose-dependent and are observed at concentrations of HGF which are assumed to be in present in proximity to intestinal epithelial cells *in vivo* (p. 707, second paragraph). Authors conclude that HGF may play a role in both regulating proliferation of gastrointestinal epithelia and morphogenesis of the gastrointestinal tract and its remodeling following injury *in vivo* (p. 707).

Similarly, Nusrat et al, using *in vitro* wound model, demonstrate that HGF influences migratory and spreading response of epithelial cells in not only cells adjoining the wound but also cells many positions removed from the wound, and thus dramatically increases the rate of epithelial wound closure. These effects provide novel therapeutic strategies to enhance repair of intestinal epithelial erosions/ulcerations. See abstract, and page 2061, bottom.

It would be *prima facie* obvious to one skilled in the art at the time the invention was made to be motivated to reduce pathological lesions (i.e. wounds) in patients suffering from inflammatory bowel disease. It would be obvious to an artisan, therefore, to be motivated to treat patients suffering from inflammatory bowel disease with HGF because both Nusrat and Dignass demonstrate that HGF stimulates two essential intestinal epithelial cell functions, proliferation and restitution, which result in wound

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restitution and because both references suggest that HGF would be useful *in vivo* to repair intestinal epithelial erosions/ulcerations.

The invention as a whole would have been *prima facie* obvious to one having ordinary skills in the art at the time the invention was made, especially in the absence of any evidence to the contrary.

The references do not expressly teach the claimed concentration ranges. Absent some teaching to the contrary however, the determination of particular ranges employed is within the skill of the ordinary worker as a part of the process of normal optimization. Note that Dignass reference emphasizes that *in vitro* effects have been observed at concentrations of HGF which are assumed to be in present in proximity to intestinal epithelial cells *in vivo*.

Conclusion.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Michael Borin, Ph.D.
Primary Examiner
Art Unit 1631

mlb